REMARKS

Claims 1-7, 9, 10, and 13-15 are pending in this application. Independent claim 1 has been amended to clarify that detection of increased HML-2 expression product levels indicates a diagnosis of prostate cancer. Support is found, for example, on page 2, lines 11-14: "This finding [of up-regulated expression] can be used in prostate cancer . . . diagnosis . . ."

Accordingly, no new matter is added.

The Rejections under 35 U.S.C. § 112, ¶ 1 (Written Description and Enablement)

Claims 1-7, 9, 10, and 13-15 stand rejected as not satisfying one or both of the written description or enablement requirements under 35 U.S.C. § 112 ¶ 1. Applicants respectfully traverse these rejections.

Independent claim 1 (and its dependent claims 2-7, 9, 10, and 13-15) are directed to a method for diagnosing prostate cancer. The method comprises detecting increased levels of an HML-2 retrovirus encoded expression product in a patient prostate or blood sample. An increased level of the expression product of at least 150% relative to a negative control sample, indicates a diagnosis of prostate cancer.

Written Description

To determine compliance with the written description requirement, the fundamental inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that Applicants were in possession of the claimed invention as of the filing date. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-1564, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). The claimed invention meets this legal standard.

One of skill in the art would readily recognize from the specification that Applicants were in possession of every element recited in the claims. As stated on pages 7-8 of Applicants' response filed December 27, 2005, the specification describes HML-2 retroviruses and provides numerous examples of sequences of HML-2 retroviruses and their RNA and polypeptide expression products. The specification also describes numerous methods for directly or indirectly detecting increased levels of HML-2 retrovirus encoded expression products. See page 9, line 27 to page 10, line 22 and page 74, line 26 to page 76, line 26. The specification further describes the detection of these expression products in a patient prostate or blood sample. See page 3, lines 7-8. The specification additionally describes the detection of an increased level of expression product, of at least 150% relative to a negative control sample, in the diagnosis of prostate cancer. See page 25, lines 17-18.

The working examples describe assaying a variety of candidate genes to be screened for their differential expression in prostate cancer. See page 74, line 26 to page 75, line 25. Using a differential expression assay, Applicants were able to identify 16 gene products that increased significantly in expression in tumor probes, relative to normal probes. See page 75, line 26 to page 76, line 26. The degree of up-regulation relative to a control for most of these gene products was $\geq$200% in at least 75% of the patients studied. See Table 6. Applicants conducted PCR analysis of these expression products, having this shared, significant degree of up-regulation in prostate tumor cells relative to normal cells. See page 76, line 27 to page 77, line 3. Applicants discovered all 16 of the gene product isolates share some degree of identity to HERV-K(II) and HERV-K(10), which are members of the HML-2 subgroup of the HERV-K family. See page 77, line 4 to page 79, line 5 and page 37, lines 4-9.

The specification thus describes HML-2 retroviruses, their expression products, and the detection of these expression products. The specification combines this overall description with detailed procedures which led to the positive identification of particular expression products which were significantly up-regulated in prostate tumor cells. From this description, there is simply no reason to doubt the ability of one of ordinary skill to routinely carry out the same screening and analysis procedures, in order to identify further (and theoretically all) HML-2 expression products which are up-regulated in prostate cancer cells. In carrying out the claimed method of diagnosing prostate cancer, such HML-2 expression products could also be detected according to the same procedures which Applicants have specifically disclosed.

It is therefore unreasonable, and inconsistent with the legal standard governing 35 U.S.C. § 112 ¶ 1, to compel Applicants to limit their invention to "only the isolated polynucleotide sequences that have actually been correlated with prostate cancer." Final Office Action at page 4, 2nd paragraph. The claimed invention is more than adequately described, without requiring Applicants to conduct more of the same experiments leading to the identification of all up-regulated polynucleotide sequences and other expression products.

The final Office Action bases its assertion of a lack of written description on "the lack of correlation between an increase in any/all HLM-2 [*sic*, HML-2] sequences as correlating with the presence of prostate cancer." The final Office Action cites Stauffer *et al.*[1] as providing "direct evidence that observing an increase in the level of HML-2 in the serum does not directly correlate with prostate cancer because the increase could also be due to testicular cancer or skin cancer (melanoma)."

The claimed invention, however, satisfies the written description requirement, regardless of whether blood samples of patients suffering from cancers other than prostate cancer show up-

[1] CANCER IMMUNITY, Vol. 4: 1-18 (2004).

regulated HML-2 expression products. As stated above, Applicants have demonstrated a strong correlation between increased HML-2 expression products and prostate cancer. That is, Applicants have shown HML-2 expression products to increase when prostate cancer is present. Whether or not HML-2 expression products are up-regulated due to other types of cancer is a completely separate issue, having no bearing on whether the claimed invention is sufficiently described. Moreover, Applicants are not claiming a method for conclusively distinguishing prostate cancer from other types of cancer in a patient. Instead, Applicants are claiming a method of diagnosing prostate cancer. As defined in the specification, diagnosis

> can range from a definite clinical diagnosis of disease to an indication that the patient should undergo further testing which may lead to a definite diagnosis. For example, the method of the invention can be used as part of a screening process, with positive samples being subjected to further analysis.

Specification at page 25, lines 20-25 (emphasis added).

A diagnosis of prostate cancer may thus be used to initially screen patients, potentially having prostate cancer, for further testing (*e.g.*, to confirm the presence of prostate cancer or preclude the presence of other types of cancers). Increased HML-2 expression products resulting from other types of cancers therefore do not render the recited "method of diagnosing prostate cancer" inoperative, as the final Office Action seems to suggest. For further clarification of this point, Applicants have amended claim 1 to recite that increased levels of an HML-2 expression product are indicative of a diagnosis of prostate cancer.

Lastly, the final Office Action asserts a lack of written description because Stauffer *et al.* teaches that *one* type of expression product from *one* particular HML-2 retrovirus is apparently not up-regulated in cancerous prostate tissue. In particular, the "level of EST expression of HERV-K 22q11 (HML-2) is higher in normal prostate tissue than in prostate cancers." For the

reasons stated previously, however, it would have been well within the capability of the ordinary skilled artisan having knowledge of the Applicants' teachings (including the detailed procedures for candidate gene screening, differential expression assaying, up-regulation detection, and isolate analysis), to determine which HML-2 retrovirus encoded expression products are up-regulated in patients having prostate cancer, and which are not. As noted above, Applicants have identified 16 gene product isolates which are all highly up-regulated in prostate cancer patients and which all share some degree of identity to members of the HML-2 subgroup of the HERV-K family. The specification provides a more than sufficient written description of the claimed invention, despite the contentions of the final Office Action regarding a single, potentially inoperative species. This is especially true since the specification provides more than adequate disclosure for one of ordinary skill to screen such inoperative species from other, operative HML-2 expression products, based on their extent of (or lack of) up-regulation.

Reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, ¶ 1 for lack of written description are respectfully requested.

Enablement

To satisfy enablement, the Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'." *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). The claimed invention meets this legal standard.

Having knowledge of Applicants' teachings, one of ordinary skill could make and use the full scope of the claimed invention with only routine experimentation. As stated in detail above, the specification describes procedures that were actually performed, as well as numerous other possible procedures, for detecting HML-2 retrovirus encoded expression products that are up-

regulated in prostate cancer. The specification therefore enables one of ordinary skill to detect HML-2 expression products in the diagnosis of prostate cancer, according to the claimed method.

In rejecting the claims for lack of enablement, the final Office Action essentially offers the same rationale stated above with respect to the rejections based on lack of written description. Namely, it is the final Office Action's position that there is no direct correlation between the up-regulation of HML-2 expression products and prostate cancer. This is apparently evidenced by (1) other types of cancer such as testicular cancer or skin cancer also being associated with an increase in HML-2 expression products and (2) a level of EST expression of HERV-K 22q11 (HML-2) that is higher in normal prostate tissue than in prostate cancers.

Again, the influence of other types of cancer on HML-2 expression does not prevent one from practicing the claimed invention, directed to diagnosing prostate cancer. If up-regulated HML-2 expression is detected, then prostate cancer is diagnosed. If the particular HML-2 expression product detected is associated with only prostate cancer, then diagnosis can mean the patient has prostate cancer. If the particular HML-2 expression product detected is associated with prostate cancer and possibly some other type of cancer, then diagnosis can alternatively mean that the patient should undergo further testing to determine whether the cancer is in fact prostate cancer. This is completely consistent with how the specification defines "diagnosis." The specification therefore enables a method for diagnosing prostate cancer, comprising detecting increased levels of an HML-2 expression product.

As to the apparently inoperative species (namely EST expression products of HERV-K 22q11 (HML-2), identified in the final Office Action), the Federal Circuit has made it clear that

> [t]he presence of inoperative embodiments within the scope of a claim does not necessarily render a claim non-enabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative with expenditure of no more effort than is normally required in the art.

Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1577 (Fed. Cir. 1984) (emphasis added). It is clearly within the capability of the ordinary skilled artisan to determine which embodiments (or HML-2 expression products) would be inoperative. As stated above, the specification in fact provides detailed procedures for carrying out a differential expression assay, in order to determine which HML-2 expression products are up-regulated in prostate cancer patients. Since the determination of both operative and inoperative embodiments requires no more than routine experimentation, the claimed method satisfies the Federal Circuit standard for enablement.

Reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, ¶ 1 for lack of enablement are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, all pending claims of this application are believed to be in condition for allowance. A written indication of the same is respectfully requested. This response is believed to completely address all of the substantive issues raised in the final Office Action mailed March 21, 2006.

Respectfully submitted,
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